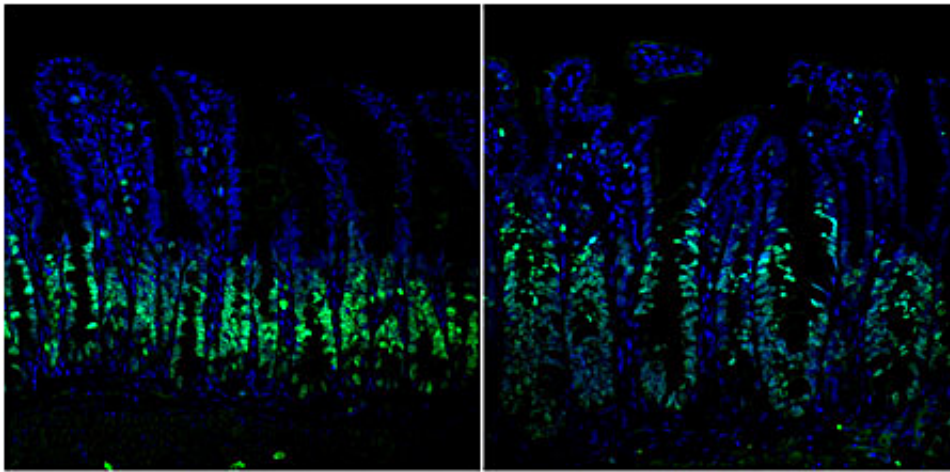


Blocking known cancer driver unexpectedly reveals a new tumor-promoting pathway

May 17 2016



Immunofluorescent staining of intestinal epithelium tissue shows cell growth (green). In a normal mouse model (left), cell growth is controlled but in a mouse model with the ERK1/2 pathway blocked (right) increased cell proliferation and loss of organization occurred. Credit: UC San Diego Health

While investigating a potential therapeutic target for the ERK1 and 2 pathway, a widely expressed signaling molecule known to drive cancer growth in one third of patients with colorectal cancer, University of California San Diego School of Medicine researchers found that an alternative pathway immediately emerges when ERK1/2 is halted, thus allowing tumor cell proliferation to continue.

"Since we were genetically deleting the ERK1/2 pathway, we expected

to see less cell proliferation," said Petrus R. de Jong, MD, PhD, a co-first author on the paper. "Instead, the opposite occurred. There was more cell growth and loss of organization within the cells."

In a paper published online May 17, 2016 in the journal *Nature Communications*, de Jong and co-first author Koji Taniguchi, MD, PhD, and colleagues, report that treating both ERK1/2 and the compensatory pathway, ERK5, concurrently with a combination of drug inhibitors halted [colorectal cancer](#) growth more effectively in both mouse models and human colorectal cancer cell lines.

The ERK pathway plays a critical role in embryonic development and tissue repair because it instructs cells to multiply and start dividing, but when over activated [cancer growth](#) occurs.

"Therapies aimed at targeting ERK1/2 likely fail because this mechanism is allowing proliferation through a different pathway," said Eyal Raz, MD, senior author and UC San Diego School of Medicine professor of medicine. "Previously, ERK5 didn't seem important in colorectal cancer. This is an underappreciated escape pathway for tumor cells. Hence, the combination of ERK1/2 and ERK5 inhibitors may lead to more effective treatments for colorectal cancer patients."

There are 1.2 million people living with this disease in the United States, making it the third most common cancer among men and women. In 2016, an estimated 134,490 new cases are expected to be diagnosed.

"If you block one pathway, cancer cells usually mutate and find another pathway that ultimately allows for a recurrence of cancer growth," said Taniguchi. "Usually, mutations occur over weeks or months. But other times, as in this case, the tumor does not need to develop mutations to find an escape route from targeted therapy. When you find the compensatory [pathway](#) and block both, there is no more escape."

Researchers suggested that other classes of inhibitors be tested in combination with ERK5 inhibitors in human colorectal cancer cells in preclinical mouse models before any patient trial can begin.

More information: Petrus R. de Jong et al, ERK5 signalling rescues intestinal epithelial turnover and tumour cell proliferation upon ERK1/2 abrogation, *Nature Communications* (2016). [DOI: 10.1038/ncomms11551](https://doi.org/10.1038/ncomms11551)

Provided by University of California - San Diego

Citation: Blocking known cancer driver unexpectedly reveals a new tumor-promoting pathway (2016, May 17) retrieved 27 April 2024 from <https://medicalxpress.com/news/2016-05-blocking-cancer-driver-unexpectedly-reveals.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.